

What is claimed is:

1. A self-calibrating scanning system for scanning a microarray of biomolecules comprising:

an excitation light source that produces an excitation light;

5 an optics portion that directs the excitation light from the excitation light source to the microarray of biomolecules;

a detection portion that produces an output signal responsive to an emission detected from a label on the microarray being scanned with the excitation light; and

10 a calibration portion that calibrates sensitivity of the detection portion, the calibration portion comprising:

a calibration apparatus that produces a calibrated light at a reference light level that is detected by the detection portion; and

15 a compensation portion that compensates for changes in the sensitivity of the detection portion, or which saves an indication of sensitivity in a memory in association with data read from the array in response to illumination with excitation light.

2. The self-calibrating scanning system of Claim 1, wherein the calibration apparatus comprises a calibration light source that consistently reproduces the calibrated light.

20 3. The self-calibrating scanning system of Claim 1, wherein the compensation portion comprises a reference value corresponding to an initial output value from the detection portion responsive to the reference light level.

4. The self-calibrating scanning system of Claim 2, wherein the calibration apparatus further comprises a calibration detector and a control in a closed loop to  
25 provide reproducibility of the calibrated light from the calibration light source.

5. The self-calibrating scanning system of Claim 1, further comprising an analysis portion that comprises one or more of a computer, a processor and memory

to collect and analyze the output signal from the detection portion and to produce information about the labeled biomolecule.

6. The self-calibrating scanning system of Claim 5, wherein the compensation portion uses a respective one or more of the computer, the processor  
5 and the memory of the analysis portion to provide an indication and a magnitude of the change in sensitivity for use with the information about the labeled biomolecule.

7. The self-calibrating scanning system of Claim 3, wherein the compensation portion further comprises one or more of a computer, a processor and memory to optionally provide an indication and a magnitude of the change in  
10 sensitivity.

8. The self-calibrating scanning system of Claim 7, wherein the compensation portion further comprises a digital to analog converter to adjust the detection portion when there is a change in sensitivity.

9. The self-calibrating scanning system of Claim 3, wherein the  
15 compensation portion further comprises a digital to analog converter to adjust the detection portion when an output value from the detection portion responsive to the calibrated light differs from the reference value.

9. The self-calibrating scanning system of Claim 3, wherein the compensation portion indicates if an output value from the detection portion  
20 responsive to the calibrated light differs from the reference value and saves a magnitude of the difference for reference.

10. The self-calibrating scanning system of Claim 7, wherein the reference value is stored in the memory, and wherein the change in sensitivity is indicated by a difference between the reference value and an output value from the detection portion  
25 responsive to the calibrated light.

11. The self-calibrating scanning system of Claim 1, wherein the excitation light source comprises one of a laser or other light source that produces the collimated light, and the detection portion comprises a photomultiplier tube detector, and the system further comprising an optional analysis portion that comprises a  
5 microprocessor.

12. The system of Claim 1, wherein the calibration portion is integral to the scanning system.

13. The system of Claim 1, wherein the calibration apparatus is integral to the scanning system.

10 14. The system of Claim 1, wherein the calibration portion further comprises one or more of an optical component and a filter, wherein the optical component efficiently distributes the calibrated light to a detector in the detection portion, and the filter attenuates signal noise from reaching the detection portion.

15 15. The system of Claim 1, wherein the calibration portion further comprises a filter to modify the calibrated light to correspond to the emission from the scanned label on the microarray.

16. The system of Claim 1, wherein the detection portion comprises multiple channels having a photomultiplier tube in each channel, and wherein the calibration portion further comprises a filter, and wherein the calibration apparatus and the filter  
20 provide different calibrated light levels from the calibration portion to the multiple channels of the detection portion.

17. The system of Claim 1, wherein the calibration apparatus comprises a plurality of calibration light sources, with different ones of the calibration light sources emitting a different calibrated light at a different reference light level that  
25 corresponds to an emission in a different spectral range from a scanned label on the microarray of biomolecules, and wherein the detection portion comprises a photomultiplier tube detector to detect the emissions in the different spectral ranges.

18. The system of Claim 1, wherein the detection portion comprises a plurality of different color channels to detect emissions in a plurality of different color spectral ranges, each different color channel comprising a photomultiplier tube detector, and wherein the calibration portion comprises a plurality of calibration apparatuses, at least one different calibration apparatus for each different color channel, such that the photomultiplier tube detector in each color channel is calibrated with one corresponding color calibrated light.

19. The system of Claim 4, wherein the calibrated light source is selected from a lamp with a filter, a solid state emitter, or a light emitting diode, the calibration detector is selected from a photodiode or phototransistor, the control is a control amplifier, and the closed loop is provided by a regulator or servomechanism.

20. A method of calibrating an scanning system used for scanning an array of biomolecules that has an excitation light source that produces a stable collimated light, an optics portion, and a detection portion comprising the steps of:  
initially calibrating the detection portion with a reference light level, the detection portion producing an initial output signal in response to the initial calibration that is stored for reference; and  
subsequently calibrating the detection portion with a calibration apparatus that produces a calibrated light at the reference light level, the detection portion producing a subsequent output signal in response to the subsequent calibration that is analyzed for calibration, or saving an indication of sensitivity in a memory in association with data read from the array in response to illumination with excitation light.

21. The method of Claim 20, wherein the step of initially calibrating comprises the steps of:  
initially generating a fixed signal corresponding to the reference light level with the calibration apparatus; and  
measuring the output signal from the detection portion in response to the initial fixed signal.

22. The method of Claim 21, wherein the steps of initially generating and measuring are repeated one or more times, the output signal from the detection portion is recorded each time, and a mean value for the initial output signal is calculated from the recorded output signals and is stored as a reference value.

5        23. The method of Claim 20, wherein the step of subsequently calibrating comprises the steps of:

          subsequently generating the calibrated light with the calibration apparatus;  
          measuring the output signal from the detection portion in response to the  
          subsequently generated calibrated light to compare the subsequent output signal to the  
10        initial output signal for changes; and  
          compensating for any changes in the subsequent output signal.

24. The method of Claim 23, wherein the step of compensating comprises adjusting the detection portion until the subsequent output signal corresponds to the initial output signal.

15        25. The method of Claim 23, wherein the step of compensating comprises providing sensitivity change data for analysis.

26. The method of Claim 23, wherein the steps of subsequently generating and measuring are repeated one or more times, the subsequent output signal from the detection portion is recorded each time, and a mean value for the subsequent output  
20        signal is calculated from the recorded output signals before the respective output signals are compared.

27. The method of Claim 24, wherein the step of adjusting comprises adjusting voltage of the detection portion.

28. The method of Claim 24, wherein the step of adjusting comprises adjusting  
25        a scale factor of the detection portion.

29. The method of Claim 24, wherein the step of adjusting comprises adjusting the gain of the detection portion.

30. The method of Claim 20, further comprising the step of:  
repeating the step of subsequently calibrating periodically.

5 31. The method of Claim 30, wherein the steps of subsequently calibrating and repeating occur automatically at predetermined times.

32. The method of Claim 20, wherein the step of subsequently calibrating occurs after a predetermined time.

10 34. The method of Claim 20, wherein the step of initially calibrating and the step of subsequently calibrating are performed at the same location.

35. The method of Claim 20, wherein the step of initially calibrating is performed at a first location and the step of subsequently calibrating is performed at a second location remote from the first location.

15 36. The method of Claim 35, wherein the step of subsequently calibrating is initiated from the first location.

20 37. The method of Claim 20, further comprising the step of scanning an array of labeled biomolecules to obtain data on the array, wherein the step of subsequently calibrating one or both of precedes or follows the step of scanning, and wherein any change in detection sensitivity is correlated with the array data in the step of subsequently calibrating.

38. The method of Claim 25, further comprising the step of scanning an array of labeled biomolecules to obtain data on the array, wherein the step of providing comprises displaying whether a sensitivity change was measured.

39. The method of Claim 38, wherein the step of providing further comprises correlating the sensitivity change data with the array data during analysis to correct the array data for any sensitivity changes.

40. In a scanning system for scanning a microarray of labeled biomolecules  
5 that has an excitation light source that produces a stable collimated light, an optics portion, and a detection portion, the improvement comprising:

a calibration portion for calibrating sensitivity of the detection portion, the calibration portion comprising:

10 a calibration apparatus that produces a calibrated light at a preselected light level that is detected by the detection portion; and

a compensation portion that measures an output value from the detection portion responsive to the calibrated light, compares the output value to a reference value to determine whether the output value is different from the reference value, and compensates for any differences.

15 41. The system of Claim 40, wherein the compensation portion compensates by adjusting the detection portion when a difference in values is determined so as to make the difference equal or approach zero.

42. The system of Claim 40, wherein the calibration portion monitors the sensitivity of the detection portion periodically.

20 43. The system of Claim 40, wherein the compensation portion compensates by providing a magnitude of difference between the output value and the reference value to an array read file for analysis.

44. The system of Claim 43, wherein the compensation portion further compensates by displaying whether a difference was determined.

25 45. The system of Claim 40, wherein the calibration portion is integral with the scanning system.

46. The system of Claim 40, wherein the calibration apparatus is integral with the scanning system.

47. The system of Claim 40, wherein the calibration apparatus comprises:  
a calibration light source that consistently reproduces the calibrated light; and  
5 optionally further comprises:  
a calibration detector that measures a signal from the calibration light source  
corresponding to the calibrated light; and  
a control connected between the calibration light source and the calibration  
detector that can adjust the calibration light source in a closed loop when needed, such  
10 that the calibration light source consistently reproduces the calibrated light at the  
preselected light level.

48. The system of Claim 40, further comprising an analysis portion, wherein all or part of the compensation portion is incorporated into the analysis portion.